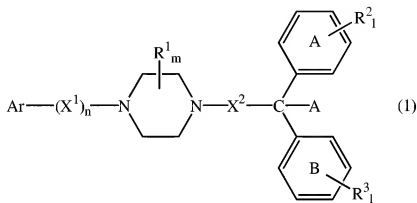


CLAIMS

(without amendment)

1. (previously presented): A method to treat pain which method comprises administering to a subject in need of such treatment an effective amount of a compound of the formula:



or a pharmaceutically acceptable salt thereof,

wherein Ar is phenyl, pyridyl, pyrimidyl, indolyl, benzimidazolyl, benzotriazolyl, isoquinolyl, quinolyl, benzothiazolyl, benzofuranyl, thienyl, furyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl or phthalimido, each of which may optionally be substituted with one or more of alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (1-16C), arylalkenyl (7-16C), each optionally containing 1-4 heteroatoms (N, O or S), O-aryl, O-alkylaryl, O-aroyl, NR-aryl, N-alkylaryl, NR-aroyl, halo, OR, NR₂, SR, -OOCR, -NROCR, RCO, -COOR, -CONR₂, and/or SO₂NR₂, wherein each R is independently H or alkyl (1-8C), and/or by -CN, OCF, -CF₃, and/or NO₂;

X¹ is a 1-5 member chain linking the piperazine to Ar;

n is 1;

each R¹-R³ is independently a alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (1-16C), arylalkenyl (7-16C), each optionally containing 1-4 heteroatoms (N, O or S), O-aryl, O-alkylaryl, O-aroyl, NR-aryl, N-alkylaryl, NR-aroyl, halo, OR, NR₂, SR, -OOCR, -NROCR, RCO, -COOR, -CONR₂, and/or SO₂NR₂, wherein each R is independently H or alkyl (1-8C), and/or by -CN, OCF, -CF₃, and/or NO₂;

each l is independently 0-5;

m is 0-4;

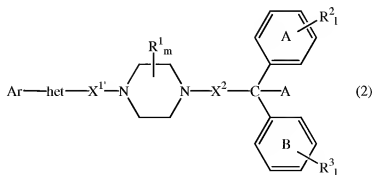
X^2 is a linker comprising a chain of at least 5 members;

A is H, OR, SR, NR_2 , or halo wherein R is H or lower alkyl (1-6C);

with the proviso that

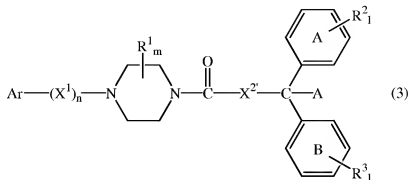
- (a) Ar is a pyridyl, pyrimidyl, indolyl, benzimidazolyl, benzotriazolyl, isoquinolyl, quinolyl, benzothiazolyl, benzofuranyl, thienyl, furyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl or phthalimido optionally substituted with one or more of alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (1-16C), arylalkenyl (7-16C), each optionally containing 1-4 heteroatoms (N, O or S), O-aryl, O-alkylaryl, O-aryol, NR -aryl, N-alkylaryl, NR -aryol, halo, OR, NR_2 , SR, $-OOCR$, $-NROCR$, RCO, $-COOR$, $-CONR_2$, and/or SO_2NR_2 , wherein each R is independently H or alkyl (1-8C), and/or by $-CN$, OCF, $-CF_3$, and/or NO_2 ; and/or
- (b) m is 1-4; and/or
- (c) X^2 is alkylene substituted by $=O$, OR, SR, NR_2 and/or halo; and/or
- (d) X^2 is a chain of at least 6 members; and/or
- (e) X^2 contains at least one heteroatom selected from N, S and O; and/or
- (f) A is OR, SR, NR_2 or halo, wherein R is H or lower alkyl (1-6C) and/or
- (g) Ar is substituted with at least one t-butyl moiety or at least one substituted alkoxy; and/or
- (h) X^1 includes at least one heteroatom selected from O, N and S.

2. (previously presented): The method of claim 1 wherein the compound of formula (1) is of the formula



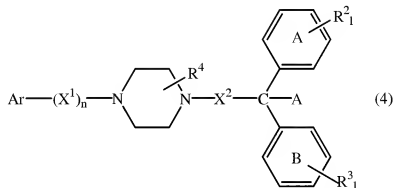
wherein Ar, R^1 - R^3 , l, m, X^2 and A are as defined above, "het" is a heteroatom selected from O, S and N, and wherein $X^{1'}$ is defined as X^1 but lacking one chain member.

3. (previously presented): The method of claim 1 wherein the compound of formula (1) is of the formula



wherein Ar, X^1 , R^1 - R^3 , l, m, n, A and Ar are defined as above, and $X^{2'}$ is defined as X^2 but lacking one chain member.

4. (previously presented): The method of claim 1 wherein the compound of formula (1) is of the formula



wherein R^4 is =O, or a carboxylic acid group or ester or amide thereof and Ar, R^2 - R^3 , X^1 , l, n, X^2 and A are defined as above.

5. (previously presented): The method of claim 1, wherein each R^1 - R^3 and optional Ar substituent is independently alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (7-16C) or arylalkenyl (7-16C) each optionally further containing 1-4 heteroatoms (N, O or S), or is halo, CF_3 , OCF, NO_2 , NH_2 , OH, or SH wherein S may optionally be oxidized.

6. (canceled)

7. (previously presented): The method of claim 1, wherein each I is independently 0 or 1.

8. (canceled)

9. (previously presented): The method of claim 1, wherein X^1 is substituted by =O at the position next to the piperazine ring.

10. (previously presented): The method of claim 1, wherein each of R^2 and R^3 is independently alkoxy, halo, or alkyl.

11. (previously presented): The method of claim 1, wherein m is 1 and R^1 is =O or a is carboxylic acid group or ester or amide thereof.

12. (previously presented): The method of claim 1, wherein Ar is optionally substituted phenyl.

13. (previously presented): The method of claim 12, wherein said phenyl is unsubstituted or is substituted by one or more tert-butyl, methoxy, substituted alkoxy, hydroxy and/or halo.

14. (previously presented): The method of claim 13, wherein the substituted alkoxy is substituted by an amino group.

15. (previously presented): The method of claim 1, wherein Ar is optionally substituted pyrimidyl, pyridyl, benzothiazole, benzimidazole or indole.

16. (previously presented): A method to treat pain which method comprises administering to a subject in need of such treatment an effective amount of a compound selected from the group consisting of

6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenylsulfanyl-ethyl)-piperazin-1-yl]-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(4-fluoro-phenoxy)-ethyl]-piperazine;

1-{4-[2-(Benzo[1,3]dioxol-5-yloxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(2-phenylsulfanyl-ethyl)-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(4-methoxy-phenoxy)-ethyl]-piperazine;

1-{4-[2-(2,4-Difluoro-phenoxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenoxy-ethyl)-piperazin-1-yl]-hexan-1-one;

1-{4-[2-(2,4-Dichloro-phenoxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(4-methoxy-phenoxy)-ethyl]-piperazin-1-yl}-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(2-phenoxy-ethyl)-piperazine;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(3,4,5-trimethoxy-phenoxy)-ethyl]-piperazin-1-yl}-hexan-1-one;

1-{4-[2-(Benzothiazol-2-ylsulfanyl)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

[4-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-ethoxy)-2,3,6-trimethyl-phenyl]-carbamic acid tert-butyl ester;

4-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethoxy)-2,3,6-trimethyl-phenylamine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(2,4-dichloro-phenoxy)-ethyl]-piperazine;

[2-(4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl})-2,6-di-tert-butyl-phenoxy)-ethyl]-dimethyl-amine;

4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-di-tert-butyl-phenol;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-methoxy-benzyl)-piperazine;

{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-(3,5-di-tert-butyl-4-methoxy-phenyl)-methanone;

1-{4-[3,5-Di-tert-butyl-4-(2-dimethylamino-ethoxy)-benzoyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-Benzo[1,3]dioxol-5-ylmethyl-4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-benzyl)-piperazine;

{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-(3,5-di-tert-butyl-4-hydroxy-phenyl)-methanone;

1-[4-(3,5-Di-tert-butyl-4-hydroxy-benzyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Dibromo-4-hydroxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-4-hydroxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-tert-butyl-benzyl)-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(9H-thioxanthen-9-yl)-piperazine;

2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-benzothiazole;

6,6-Bis-(4-fluoro-phenyl)-1-(4-pyrimidin-2-yl-piperazin-1-yl)-hexan-1-one;

2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-pyrimidine;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(9H-thioxanthen-9-yl)-piperazin-1-yl]-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid ethyl ester;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(3,4,5-trimethoxy-benzylamino)-ethyl]-piperazin-1-yl}-hexan-1-one;

9,9-Bis-(4-fluoro-phenyl)-1-[4-(3,4,5-trimethoxy-benzyl)-piperazin-1-yl]-nonan-1-one;

(2-[4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl]-ethyl)-phenyl-amine;

1-[9,9-Bis-(4-fluoro-phenyl)-nonyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine;

(4-[4-[Bis-(4-fluoro-phenyl)-methoxy]-butyl]-piperazin-1-yl)-(3,4,5-trimethoxy-phenyl)-methanone;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(4-trifluoromethoxy-benzoyl)-piperazin-1-yl]-hexan-2-one;
1-[4-(4-Bromo-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;
6,6-Bis-(4-fluoro-phenyl)-5-hydroxy-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-
hexan-1-one;
1-[4-[Bis-(4-fluoro-phenyl)-methoxy]-butyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine;
6,6-Bis-(4-fluoro-phenyl)-6-hydroxy-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-
hexan-1-one;
4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-1-(3,4,5-trimethoxy-benzyl)-piperazine-2-
carboxylic acid;
4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,4,5-trimethoxy-benzyl)-piperazin-2-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-4-(3,5-di-tert-butyl-4-methoxy-benzoyl)-
piperazin-2-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzoyl)-piperazin-2-one;
4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-1-(3,4,5-trimethoxy-benzyl)-piperazin-2-one;
4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,5-di-tert-butyl-4-methoxy-benzyl)-
piperazin-2-one;
4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-[2-(4-fluoro-phenoxy)-ethyl]-piperazin-2-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-methoxy-benzoyl)-
piperazin-2-one;
4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,5-di-tert-butyl-4-methoxy-benzoyl)-
piperazin-2-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-methoxy-benzoyl)-piperazin-2-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-4-(3,5-di-tert-butyl-4-hydroxy-benzoyl)-
piperazin-2-one;
6,6-Bis-(4-fluoro-phenyl)-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-hex-5-en-1-one;
1-[4-[2-(3,4-Dimethoxy-phenoxy)-ethyl]-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-
hexan-1-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(3,4-dimethoxy-phenoxy)-ethyl]-piperazine;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine-2-
carboxylic acid;

4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-1-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid ethyl ester;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4-dimethoxy-benzyl)-piperazine;

1-[4-(3,4-Dimethoxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[2-(Benzo[1,3]dioxol-5-yloxy)-ethyl]-4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(3,4,5-trimethoxy-phenoxy)-ethyl]-piperazine;

1-(4-Amino-2,3,5-trimethyl-phenoxy)-3-{4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-propan-2-ol;

1-{4-[3-(4-Amino-2,3,5-trimethyl-phenoxy)-2-hydroxy-propyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-(4-Benzothiazol-2-yl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-bis-trifluoromethyl-benzyl)-piperazine;

1-[4-(3,5-Bis-trifluoromethyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(4-tert-Butyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-bromo-benzyl)-piperazine;

2-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethylsulfanyl)-benzothiazole;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(4-hydroxy-3,5-dimethoxy-benzoyl)-piperazin-1-yl]-hexan-1-one;

4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-dibromo-phenol;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-trifluoromethoxy-benzyl)-piperazine;

(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethyl)-(3,4,5-trimethoxy-benzyl)-amine;

1-{4-[2-(4-Fluoro-phenoxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenylamino-ethyl)-piperazin-1-yl]-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(2,4-difluoro-phenoxy)-ethyl]-piperazine;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-chloro-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-methylbenzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-isopropylbenzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-tert-butylbenzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-fluorobenzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-chlorobenzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-methylbenzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-isopropylbenzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-tert-butylbenzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-fluorobenzamide;

1-[4-(2-Benzylamino-ethyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-{4-[2-(4-Chloro-benzylamino)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(4-methyl-benzylamino)-ethyl]-piperazin-1-yl}-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(4-isopropyl-benzylamino)-ethyl]-piperazin-1-yl}-hexan-1-one;

1-{4-[2-(4-tert-Butyl-benzylamino)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-{4-[2-(4-Fluoro-benzylamino)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(1-hydroxy-pyridine-4-carbonyl)-piperazin-1-yl]-hexan-1-one;

4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-dimethoxy-phenol;

9,9-Diphenyl-1-[4-(3,4,5-trimethoxy-benzyl)-piperazin-1-yl]-nonan-1-one;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

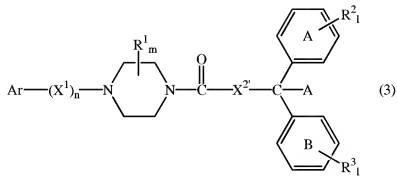
1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-3-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one; and

1-[4-(4-tert-Butyl-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one, including the pharmaceutically acceptable salts thereof.

17-18. (canceled)

19. (previously presented): A compound of the formula



wherein Ar is phenyl, pyridyl, pyrimidyl, indolyl, benzimidazolyl, benzotriazolyl, isoquinolyl, quinolyl, benzothiazolyl, benzofuranyl, thienyl, furyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl or phthalimido, each of which may optionally be substituted with one or more alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (1-16C), arylalkenyl (7-16C), each optionally containing 1-4 heteroatoms (N, O or S), O-aryl, O-alkylaryl, O-aroyle, NR-aryl, N-alkylaryl, NR-aroyle, halo, OR, NR₂, SR, -OOCR, -NROCR, RCO, -COOR, -CONR₂, and/or SO₂NR₂, wherein each R is independently H or alkyl (1-8C), and/or by -CN, OCF, -CF₃, and/or NO₂;

X¹ is a 1-5 member chain linking the piperazine to Ar;

n is 1;

each R¹-R³ is independently a alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (1-16C), arylalkenyl (7-16C), each optionally containing 1-4 heteroatoms (N, O or S), O-aryl, O-alkylaryl, O-aroyle, NR-aryl, N-alkylaryl, NR-aroyle, halo, OR, NR₂, SR, -OOCR, -NROCR, RCO, -COOR, -CONR₂, and/or SO₂NR₂, wherein each R is independently H or alkyl (1-8C), and/or by -CN, OCF, -CF₃, and/or NO₂;

each l is independently 0-5;

m is 0-4;

X² is a linker comprising a chain of at least 4 members;

A is H, OR, SR, NR₂, or halo wherein R is H or lower alkyl (1-6C);

with the proviso that

(a) Ar is a pyridyl, pyrimidyl, indolyl, benzimidazolyl, benzotriazolyl, isoquinolyl, quinolyl, benzothiazolyl, benzofuranyl, thienyl, furyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl or phthalimido optionally substituted with one or more of alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (1-16C), arylalkenyl (7-16C), each optionally containing 1-4 heteroatoms (N, O or S), O-aryl, O-alkylaryl, O-aroyle, NR-aryl, N-alkylaryl, NR-aroyle, halo, OR, NR₂, SR, -OOCR, -NROCR, RCO, -COOR, -CONR₂, and/or SO₂NR₂, wherein each R is independently H or alkyl (1-8C), and/or by -CN, OCF, -CF₃, and/or NO₂; and/or

(b) m is 1-4; and/or

(c) X² is alkylene substituted by =O, OR, SR, NR₂ and/or halo; and/or

(d) X² is a chain of at least 6 members; and/or

- (e) X^2 contains at least one heteroatom selected from N, S and O; and/or
- (f) A is OR, SR, NR_2 or halo, wherein R is H or lower alkyl (1-6C) and/or
- (g) Ar is substituted with at least one t-butyl moiety or at least one substituted alkoxy; and/or
- (h) X^1 includes at least one heteroatom selected from O, N and S.

20. (previously presented): The compound of claim 19, wherein each R^1 - R^3 and optional Ar substituent is independently alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (7-16C) or arylalkenyl (7-16C) each optionally further containing 1-4 heteroatoms (N, O or S), or is independently, halo, CF_3 , OCF, NO_2 , NH_2 , OH, or SH wherein S may optionally be oxidized.

21. (previously presented): The compound of claim 19, wherein each l is independently 0 or 1.

22. (previously presented): The compound of claim 19, wherein X^1 is substituted by =O at the position next to the piperazine ring.

23. (previously presented): The compound of claim 19, wherein each of R^2 and R^3 is independently alkoxy, halo, or alkyl.

24. (previously presented): The compound of claim 19, wherein m is 1 and R^1 is =O or a carboxylic acid group or ester or amide thereof.

25. (previously presented): The compound of claim 19, wherein Ar is optionally substituted phenyl.

26. (previously presented): The compound of claim 25, wherein said phenyl is unsubstituted or is substituted by one or more tert-butyl, methoxy, substituted alkoxy, hydroxy and/or halo.

27. (previously presented): The compound of claim 26, wherein the substituted alkoxy is substituted by an amino group.

28. (previously presented): The compound of claim 19, wherein Ar is optionally substituted pyrimidyl, pyridyl, benzothiazole, benzimidazole or indole.

29. (previously presented): A compound selected from the group consisting of
6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenylsulfanyl-ethyl)-piperazin-1-yl]-hexan-1-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(4-fluoro-phenoxy)-ethyl]-piperazine;
1-[4-[2-(Benzo[1,3]dioxol-5-yloxy)-ethyl]-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-
hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(2-phenylsulfanyl-ethyl)-piperazine;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(4-methoxy-phenoxy)-ethyl]-piperazine;
1-[4-[2-(2,4-Difluoro-phenoxy)-ethyl]-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-
hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenoxy-ethyl)-piperazin-1-yl]-hexan-1-one;
1-[4-[2-(2,4-Dichloro-phenoxy)-ethyl]-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-
hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-[2-(4-methoxy-phenoxy)-ethyl]-piperazin-1-yl]-
hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(2-phenoxy-ethyl)-piperazine;
6,6-Bis-(4-fluoro-phenyl)-1-[4-[2-(3,4,5-trimethoxy-phenoxy)-ethyl]-piperazin-1-yl]-
hexan-1-one;

1-[4-[2-(Benzothiazol-2-ylsulfanyl)-ethyl]-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-
hexan-1-one;

[4-(2-[4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl]-ethoxy)-2,3,6-trimethyl-
phenyl]-carbamic acid tert-butyl ester;

4-(2-[4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl]-ethoxy)-2,3,6-trimethyl-
phenylamine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(2,4-dichloro-phenoxy)-ethyl]-piperazine;

[2-(4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-di-tert-butyl-phenoxy)-ethyl]-dimethyl-amine;

4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-di-tert-butyl-phenol;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-methoxy-benzyl)-piperazine;

{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-(3,5-di-tert-butyl-4-methoxy-phenyl)-methanone;

1-{4-[3,5-Di-tert-butyl-4-(2-dimethylamino-ethoxy)-benzoyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-Benzol[1,3]dioxol-5-ylmethyl-4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-benzyl)-piperazine;

{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-(3,5-di-tert-butyl-4-hydroxy-phenyl)-methanone;

1-[4-(3,5-Di-tert-butyl-4-hydroxy-benzyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Dibromo-4-hydroxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-4-hydroxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-tert-butyl-benzyl)-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(9H-thioxanthen-9-yl)-piperazine;

2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-benzothiazole;

6,6-Bis-(4-fluoro-phenyl)-1-(4-pyrimidin-2-yl-piperazin-1-yl)-hexan-1-one;

2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-pyrimidine;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(9H-thioxanthen-9-yl)-piperazin-1-yl]-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid ethyl ester;

6,6-Bis-(4-fluoro-phenyl)-1-[4-[2-(3,4,5-trimethoxy-benzylamino)-ethyl]-piperazin-1-yl]-hexan-1-one;

9,9-Bis-(4-fluoro-phenyl)-1-[4-(3,4,5-trimethoxy-benzyl)-piperazin-1-yl]-nonan-1-one;

(2-[4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl]-ethyl)-phenyl-amine;

1-[9,9-Bis-(4-fluoro-phenyl)-nonyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine;

(4-[4-[Bis-(4-fluoro-phenyl)-methoxy]-butyl]-piperazin-1-yl)-(3,4,5-trimethoxy-phenyl)-methanone;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(4-trifluoromethoxy-benzoyl)-piperazin-1-yl]-hexan-2-one;

1-[4-(4-Bromo-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-5-hydroxy-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-hexan-1-one;

1-[4-[Bis-(4-fluoro-phenyl)-methoxy]-butyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine;

6,6-Bis-(4-fluoro-phenyl)-6-hydroxy-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-hexan-1-one;

4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-1-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid;

4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,4,5-trimethoxy-benzyl)-piperazin-2-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-4-(3,5-di-tert-butyl-4-methoxy-benzoyl)-piperazin-2-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzoyl)-piperazin-2-one;

4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-1-(3,4,5-trimethoxy-benzyl)-piperazin-2-one;

4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,5-di-tert-butyl-4-methoxy-benzyl)-piperazin-2-one;

4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-[2-(4-fluoro-phenoxy)-ethyl]-piperazin-2-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-methoxy-benzoyl)-piperazin-2-one;

4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,5-di-tert-butyl-4-methoxy-benzoyl)-piperazin-2-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-methoxy-benzyl)-piperazin-2-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-4-(3,5-di-tert-butyl-4-hydroxy-benzoyl)-
piperazin-2-one;
6,6-Bis-(4-fluoro-phenyl)-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-hex-5-en-1-one;
1-{4-[2-(3,4-Dimethoxy-phenoxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-
hexan-1-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(3,4-dimethoxy-phenoxy)-ethyl]-piperazine;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine-2-
carboxylic acid;
4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-1-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic
acid ethyl ester;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4-dimethoxy-benzyl)-piperazine;
1-[4-(3,4-Dimethoxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;
1-[2-(Benzo[1,3]dioxol-5-yloxy)-ethyl]-4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazine;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(3,4,5-trimethoxy-phenoxy)-ethyl]-piperazine;
1-(4-Amino-2,3,5-trimethyl-phenoxy)-3-{4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-
yl}-propan-2-ol;
1-{4-[3-(4-Amino-2,3,5-trimethyl-phenoxy)-2-hydroxy-propyl]-piperazin-1-yl}-6,6-bis-(4-
fluoro-phenyl)-hexan-1-one;
1-(4-Benzothiazol-2-yl)-piperazin-1-yl)-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-bis-trifluoromethyl-benzyl)-piperazine;
1-[4-(3,5-Bis-trifluoromethyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-
hexan-1-one;
1-[4-(4-tert-Butyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-bromo-benzyl)-piperazine;
2-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethylsulfanyl)-benzothiazole;
6,6-Bis-(4-fluoro-phenyl)-1-[4-(4-hydroxy-3,5-dimethoxy-benzoyl)-piperazin-1-yl]-
hexan-1-one;
4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-dibromo-phenol;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-trifluoromethoxy-benzyl)-piperazine;

(2-[4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl]-ethyl)-(3,4,5-trimethoxy-benzyl)-amine;

1-[4-[2-(4-Fluoro-phenoxy)-ethyl]-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenylamino-ethyl)-piperazin-1-yl]-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(2,4-difluoro-phenoxy)-ethyl]-piperazine;

N-(2-[4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl]-2-oxo-ethyl)-benzamide;

N-(2-[4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl]-2-oxo-ethyl)-4-chloro-benzamide;

N-(2-[4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl]-2-oxo-ethyl)-4-methyl-benzamide;

N-(2-[4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl]-2-oxo-ethyl)-4-isopropyl-benzamide;

N-(2-[4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl]-2-oxo-ethyl)-4-tert-butyl-benzamide;

N-(2-[4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl]-2-oxo-ethyl)-4-fluoro-benzamide;

N-(2-[4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl]-2-oxo-ethyl)-benzamide;

N-(2-[4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl]-2-oxo-ethyl)-4-chloro-benzamide;

N-(2-[4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl]-2-oxo-ethyl)-4-methyl-benzamide;

N-(2-[4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl]-2-oxo-ethyl)-4-isopropyl-benzamide;

N-(2-[4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl]-2-oxo-ethyl)-4-tert-butyl-benzamide;

N-(2-[4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl]-2-oxo-ethyl)-4-fluoro-benzamide;

1-[4-(2-Benzylamino-ethyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-[2-(4-Chloro-benzylamino)-ethyl]-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(4-methyl-benzylamino)-ethyl]-piperazin-1-yl}-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(4-isopropyl-benzylamino)-ethyl]-piperazin-1-yl}-hexan-1-one;

1-{4-[2-(4-tert-Butyl-benzylamino)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-{4-[2-(4-Fluoro-benzylamino)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(1-hydroxy-pyridine-4-carbonyl)-piperazin-1-yl]-hexan-1-one;

4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-dimethoxy-phenol;

9,9-Diphenyl-1-[4-(3,4,5-trimethoxy-benzyl)-piperazin-1-yl]-nonan-1-one;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-3-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one; and

1-[4-(4-tert-Butyl-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one, including the pharmaceutically acceptable salts thereof.

30. (previously presented): A pharmaceutical composition which comprises, in admixture with a pharmaceutically acceptable excipient, a unit dosage amount of at least one compound of claim 19.

31. (previously presented): A pharmaceutical composition which comprises, in admixture with a pharmaceutically acceptable excipient, a unit dosage amount of at least one compound of claim 29.